

**REMARKS**

**Obviousness Rejection over Ueno '174**

On page 3 of the Office Action, claims 1, 6-16 and 18-21, 24, 25, 27 and 28 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ueno et al. (U.S. Pat. No. 6,583,174).

In response, Applicant submits initially that the present invention is entitled to the July 3, 2003 filing date of USAN 60/484,304. Thus, Applicant submits that U.S. Pat. No. 6,583,174 ("Ueno '174") is not prior art under 35 U.S.C. 102(b) because its June 24, 2003 issue date is not more than one year before the July 3, 2003 filing date of USAN 60/484,304. Rather, Ueno '174 is potentially prior art only under 35 U.S.C. 102(a) and (e) for purposes of this obviousness rejection.

With respect to Ueno '174 as potential prior art under 35 U.S.C. 102(e) for purposes of this obviousness rejection, Applicant submits that the subject matter of Ueno '174 and the presently claimed invention were, at the time the presently claimed invention was made, owned by or subject to an obligation of assignment to Sucampo AG. Thus, Applicant submits that Ueno '174 is not prior art under 35 U.S.C. 102(e) for purposes of obviousness, based on the provisions of 35 U.S.C. 103(c).

As to Ueno '174 as potential prior art under 35 U.S.C. 102(a) for purposes of this obviousness rejection, Applicant submits herewith a Rule 132 Declaration stating that Applicant was responsible for any disclosure of the present invention in Ueno '174 (an executed version of the Declaration will be submitted promptly after it is received). Thus, any disclosure of the present invention in Ueno '174 was not "before the invention thereof" by Applicant as required

by 35 U.S.C. 102(a). Thus, Applicant submits that Ueno '174 is not prior art under 35 U.S.C. 102(a).

Accordingly, Applicant submits that the present invention is not obvious over Ueno '174, and withdrawal of this rejection is respectfully requested.

### **Obviousness Rejection over EP '651**

On page 5 of the Office Action, claims 1, 6-16 and 18-28 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ueno et al. (EP 0979651).

In response, Applicant notes initially that in paragraph [0060] on page 6 of EP 0979651 ("EP '651"), it is stated that the solid composition for oral administration used according to the invention "includes tablets, troches, capsules, pills, powders, granules and the like." Further, it is stated that tablets or pills "may be gastric- or enteric-coated preparation, may be that formed by adsorbing the active ingredient to a material which allows sustained release of the ingredient, or may be in the form of micro-capsules."

Further, while 13,14-dihydro-15-keto-16,16-difluoro-18S-methyl-prostaglandin E1 is mentioned in EP '651 (see paragraph [0065], for example), a large family of further 15-keto-prostaglandin compounds is disclosed as well.

Thus, Applicant submits that in order to arrive at the claimed subject matter, one of ordinary skill in the art needs to make a multiple selection.

Applicant submits that the present invention is based on the discovery that, as shown in the examples of the present application, more than 5% of the bicyclic tautomer (as defined in the claims) is converted into the corresponding monocyclic tautomer under the condition of pH 2.

The data suggests that by protecting the bicyclic tautomer from the acidic condition, such as gastric juice, with an enteric coating, ring-opening of the bicyclic compound under this condition is effectively prevented, and the ratio of the bicyclic tautomer is effectively kept.

Further, it is worth noting that, as shown in US 6,414,016 cited on page 20, line 17 of the present application, the higher the bicyclic ratio, the higher the enteropooling effect and, therefore, the cathartic effect.

Hence, according to the present invention, the compound in the form of the bicyclic tautomer will be transported after its administration into the intestine and can act locally there.

In addition, the side effects associated with the administration of the bicyclic compound, such as irritation, will substantially be prevented by formulating the bicyclic compound as an enteric coated product.

In other words, the present invention can provide an enteric coated composition for oral administration of a specific chloride channel opener which can provide improved pharmaceutical effects for the patient to be treated. The enteric coated composition is also beneficial to prevent irritation of the upper gastric organs, such as nausea, vomiting and acid reflux, and to subsequently reduce adverse side effects due to the irritation caused by the prostaglandin compound.

As there is no teaching or suggestion in the prior art motivating one of ordinary skill in the art seeking to achieve the above mentioned desirous effects to formulate the compound recited in the instant claims so that it is not released in the stomach and to pick up the specific combination of this compound and an enteric coating, Applicant submits that the claimed invention is not obvious over EP '651.

In addition, Applicant submits that EP '651 discloses the treatment of portal hypertension, and in order to treat this disease or condition, the active ingredient is required only to achieve access to the portal vein. As is well known to the art, blood from the stomach, the intestines and some other organs flows thorough the portal vein to the liver, and therefore, there is no motivation to choose an enteric coating for providing the effect to treat portal hypertension. That is, one of ordinary skill in the art would consider that active ingredient absorbed from stomach would be effective for the treatment of portal hypertension (the disease disclosed in EP '651), and thus one would not have been motivated to use an enteric coating as in the present invention.

Thus, Applicant submits that the present invention is not obvious over EP '651, and withdrawal of this rejection is respectfully requested.

### **Obviousness Rejection over WO '912**

On page 8 of the Office Action, claims 1, 6-16 and 18-28 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ueno et al. (WO 03/030912).

In response, Applicant submits initially that the present invention is entitled to the July 3, 2003 filing date of USAN 60/484,304. Thus, Applicant submits that WO 03/030912 ("WO '912") is not prior art under 35 U.S.C. 102(b) because its April 17, 2003 publication date is not more than one year before the July 3, 2003 filing date of USAN 60/484,304. Rather, WO '912 is potentially prior art only under 35 U.S.C. 102(a) and (e) for purposes of this obviousness rejection.

With respect to WO '912 as potential prior art under 35 U.S.C. 102(e) for purposes of this obviousness rejection, Applicant submits that the subject matter of WO '912 and the presently

claimed invention were, at the time the presently claimed invention was made, owned by or subject to an obligation of assignment to Sucampo AG. Thus, Applicant submits that WO '912 is not prior art under 35 U.S.C. 102(e) for purposes of obviousness, based on the provisions of 35 U.S.C. 103(c).

As to WO '912 as potential prior art under 35 U.S.C. 102(a) for purposes of this obviousness rejection, Applicant directs the Examiner's attention to the Rule 132 Declaration submitted herewith stating that Applicant was responsible for any disclosure of the present invention in WO '912. Thus, any disclosure of the present invention in WO '912 was not "before the invention thereof" by Applicant as required by 35 U.S.C. 102(a). Thus, Applicant submits that WO '912 is not prior art under 35 U.S.C. 102(a).

Accordingly, Applicant submits that the present invention is not obvious over WO '912, and withdrawal of this rejection is respectfully requested.

## **Conclusion**

In view of the above, reconsideration and allowance of this application are now believed to be in order, and such actions are hereby solicited. If any points remain in issue which the Examiner feels may be best resolved through a personal or telephone interview, the Examiner is kindly requested to contact the undersigned at the telephone number listed below.

RESPONSE UNDER 37 C.F.R. § 1.116  
Appln. No.: 10/562,637

Attorney Docket No.: Q76459

The USPTO is directed and authorized to charge all required fees, except for the Issue Fee and the Publication Fee, to Deposit Account No. 19-4880. Please also credit any overpayments to said Deposit Account.

Respectfully submitted,



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**23373**

CUSTOMER NUMBER

Date: April 6, 2011